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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/662,812	09/15/2000	Andrew D. Murdin	032931/0235	1714

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EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 10/23/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/662,812	Murden et al
Examiner	**Art Unit**
Portner	1645

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 1, 2002*.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above, claim(s) *3-6, 9, and 13-37* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 7, 8, and 10-12* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☒ Claims *1-37* are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *4,7*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-37 are pending.

Claims 1-2(a), 7a (dependent from claim 1(a))-8a(dependent from claim 1(a)) and 10a(dependent from claim 1(a)) and 12a(dependent from claim 7, and 1(a)) are under consideration.

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged, provisional Application 60/154,652, filed September 20, 1999.

Information Disclosure Statement

2. The information disclosure statement filed December 15, 2000 and November 21, 2002 have been considered.

Sequence Letter

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

4. APPLICANT IS GIVEN THE time period set for THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response.

Please Note: Figure 2 recites sequences that fall within the sequence rules and must be assigned a SEQ ID NO. Amendment of the Brief Description of the Drawings, the Figure, or both could meet this requirement.

Election/Restriction

5. Applicant's election with traverse of Group I claims 1-14, 19, 35 and 36 are, drawn to DNA, vector, host cell, probes, primers, classified in class 536, subclass 23.1; specifically species (1) drawn to SEQ ID No 1 and 2 (claims 1-2(a), 7, 8 (no optional second nucleic acid vector), 10, 11 12);. in Paper No. 10 is acknowledged. The traversal is on the ground(s) that:

"the subject matter of the claims is sufficiently related that a thorough search for the subject matter of a single independent claim would necessarily encompass a search for the subject matter of the remaining claims;

"the search and examination of the entire application could be performed without serious burden" . These arguments have been fully considered but are not found to be persuasive for the reasons below; and

" the six allegedly distinct species of Group I is not unduly burdensome".

6. These arguments have been fully considered but are not found to be persuasive for the reasons below.

First, the classification system has no statutory recognition whether inventions are independent and distinct. For example, each class and subclass is comprised of numerous completely independent and distinct inventions.

Second, MPEP 803 states that restriction is proper between patentably distinct inventions where the inventions are (1)independent or distinct as claimed and (2) a serious search and examination burden is placed on the examiner if restriction is not required.

The term "distinct" is defined to mean that two or more subjects as disclosed are related, for example, as product and method of use, but are capable of separate manufacture, use or sale as claimed, and are patentable over each other (see MPEP 802.1). In the instant situation, the inventions of Groups I-IX are drawn to distinct inventions which are related as separate products

capable of separate functions. Restrictions between the inventions is deemed to be proper for the reason previously set forth.

In regard to burden of search and examination, MPEP 803 states that a burden can be shown if the examiner shows either separate classification, different field of search or separate status in the art. In the instant case a burden has been established in showing that the inventions of Groups I-IX are classified separately necessitating different searches of issued US Patents. In addition, anti-sense nucleic acid molecule are recognized as evidencing a distinct function that differs from that of a coding sequence of an open reading frame. Probes and primer are generally fragments of a whole, and do not encode for proteins with a three dimensional amino acid structure, as would a complete open reading frame for a protein. A nucleic acid that encodes a fusion polypeptide would evidence different biological and structural characteristics from those of a nucleic acid that only encodes a single coding sequence. However, classification of subject matter is merely one indication of the burdensome nature of search. The literature search, particularly relevant in this art, is not co-extensive, because for example DNA vaccines using coding sequences for an open reading frame would differ from that of administration of an anti-sense nucleic acid.

Additionally, it is submitted that the inventions of Groups I-IX have acquired a separate status in the art. Clearly different searches and issues are involved in the examination of each Group. For these reasons the restriction requirement is deemed to be proper and is therefore made Final.

Claim Objections

7. Claims 1-2, 7-8, 10 and 12 are objected to because of the following informalities: All of the claims recite non-elected inventions. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claims 1-2 and 7 are directed to nucleic acid molecules that have not been isolated and purified and therefore reads on a product of nature; the claimed invention is directed to non-statutory subject matter.

Claim Rejections - 35 U.S.C. § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 1(a), 8, 10-11 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid molecule that comprises a nucleic acid sequence of SEQ ID NO 1 and encodes SEQ ID No 2, does not reasonably provide enablement for the utilization of the nucleic acid molecule as a vaccine or pharmaceutical composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification discloses an isolated nucleic acid molecule of Chlamydia pneumonia that comprises SEQ ID NO 1 and encodes SEQ ID NO 2, wherein the nucleic acid molecule would be useful and able to detect the presence or absence of Chlamydia pneumonia in a

sample and for the production of an immunogenic polypeptide for induction of an immune response, the immune response being one that could be used to purify a polypeptide associated with a known human pathogen, but does not show the nucleic acid to induce a protective immune response that prevents establishment of infection and disease when in any vector or amount of nucleic acid is used to induce an immune response, nor has it been shown to induce a protective immune response to eradicate established pre-existing infection.

The specification fails to teach how to formulate and use the claimed vaccines or pharmaceutical compositions. The term "vaccine" encompasses the ability of the specific antigen to induce protective immunity to infection or disease induction.

The art teaches Chlamydia compositions when administered to an immunocompetent host induce both an immune response, as well as deleterious immune effects (see Biodrugs, 2002, abstract). Biodrugs 2002, teaches that "the development of an effective adjuvant, delivery vehicle or system for a potential subunit vaccine is still an elusive objective" for Chlamydia vaccines.

Penttila et al (Vaccine, 2002) teaches a DNA based composition that encoded an outer membrane protein (momp2) of Chlamydia pneumonia induced a "strong serum antibody response against OMP2 protein, it failed to protect the mice" against the severe effects associated with Chlamydial pneumonia. Prior to the experiments of Penttila et al, Allen et al (1993) found that OMP3 of Chlamydia was not able to prime Balb/c mice for an anamnestic immune response but OMP2 was. Despite the ability of OMP2 to induce an anamnestic immune response, the antibodies induced were shown not to be sufficiently protective for the immunized mice.

Pal et al (1999) teaches that vaccination of a mammal with DNA plasmids coding for a major Chlamydial outer membrane protein elicited an immune response but failed to protect against infection or disease by the pathogen (abstract).

Hechard et al (2002) teaches a DNA plasmid composition that induced a specific humoral immune response in a mammal, but the IgG2a antibodies failed to have any in vitro neutralizing and the spleens of the vaccinated animals were not protected (Veterinary research abstract). Bailey et al (1993) found that IgG antibodies are not protective for Chlamydial infection of the eye.

Stuart et al (1989) teaches that infected patients with Chlamydial infection have IgG antibodies circulating in their serum but remain infected and evidence disease.

The specification does not provide substantive evidence that the claimed vaccines are capable of inducing protective immunity. This demonstration is required for the skilled artisan to be able to use the claimed vaccines for their intended purpose of preventing infections. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed vaccines, i.e. would not be able to accurately predict if protective immunity has been induced.

The ability to reasonably predict the capacity of a single bacterial immunogen to induce protective immunity from in vitro antibody reactivity studies is problematic.

Ellis exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of the at protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies"(page 572, second full paragraph).

Unfortunately, the art is replete with instances where even well characterized antigens that induce an in vitro neutralizing antibody response fail to elicit in vivo protective immunity. See Boslego et al. wherein a single gonococcal pillin protein fails to elicit protective immunity even though a high level of serum antibody response I s induced (page 212, bottom of column 2). Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful vaccine without the prior demonstration of vaccine efficacy.

Further, the specification fails to provide an adequate written description of other nucleic acid molecules that would evidence the recited functional limitations of being able to induce a protective immune response, the skilled artisan would be required to de novo locate, identify and characterize the claimed nucleic acid molecules able to induce protective immune response. In light of the art established lack of predictability of vaccines, specifically Chlamydial vaccines, the skilled artisan would be required to carry out undue experimentation to identify nucleic acid molecules that would evidence the recited ability to induce a protective immune response (vaccine or pharmaceutical composition) absent specific guidance and teaching in the instant specification. The claimed invention is enabled for immunogenic compositions.

Claim Rejections - 35 U.S.C. § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

13. Claims 1-2, 7-8, 10-12 (in so far as the claims are directed to SEQ ID NO 1, a nucleic acid that encodes SEQ ID No 2, a vector and host cell that comprises SEQ ID NO 1 or encodes SEQ ID No 2) are rejected under 35 U.S.C. 102(a) as being anticipate by Kalman et al (April 1999).

The claimed invention is directed to a nucleic acid molecule that comprises SEQ ID No 1 or a nucleic acid molecule that encodes a polypeptide of SEQ ID NO 2.

Kalman et al disclose a nucleic acid molecule that comprises SEQ ID No 1 or a nucleic acid molecule that encodes a polypeptide of SEQ ID NO 2 (see sequence alignment provided which shows 100% sequence identity with SEQ ID NO 1 and would therefore encode SEQ ID NO 2; AE001587; and methods section, page 388, col. 2).

The disclosed nucleic acid molecule was obtained from Chlamydia pneumoniae strain CWL029, the nucleic acid molecule being one that is in association with expression control sequences in genomic DNA, and in association with a second nucleic acid molecule encoded by Chlamydia pneumoniae (the nucleic acid molecule being 16,448 nucleotides in length which encodes several outer membrane proteins; see alignment provided). The host cell for the cloned DNA was M13, and was contained in a pharmaceutically acceptable carrier in light of the fact that the clones remained viable and expressed the encoded nucleic acid molecule. The reference anticipates the instantly claimed invention.

Conclusion

14. This is a non-final action.

15. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

16. WO99/27105 (June 1999) is cited to show Chlamydia pneumoniae genomic sequences, primers, probes and open reading frame nucleic acid molecules (see sequence alignment attached.) Stephens et al (Science, October 23, 1998) is cited to show a nucleic acid molecule that shares 100% sequence identity with SEQ ID No 1, and 53% homology with SEQ ID NO 2 over 566 amino acids, obtained from Chlamydia trachomatis.

17. Brunham (WO98/02546) is cited to show DNA immunization against Chlamydia infection utilizing a nucleic acid coding sequence for an outer membrane protein of Chlamydia in a vector that comprises a eukaryotic promoter.

18.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ginny Portner whose telephone number is (703)308-7543. The examiner can normally be reached on Monday through Friday from 7:30 AM to 5:00 PM except for the first Friday of each two week period. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for this group is (703) 308-4242. The Group and/or Art Unit location of your application in the PTO will be Group Art Unit 1645. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to this Art Unit.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Vgp
September 10, 2002

MARK NAVARRO
PRIMARY EXAMINER